Multistate Study of the Epidemiology of Clubfoot

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BACKGROUND: Although clubfoot is a common birth defect, with a prevalence of approximately 1 per 1000 livebirths, the etiology of clubfoot remains largely unknown. Studies of the prevalence and risk factors for clubfoot in the United States have previously been limited to specific states. The purpose of this study was to pool data from several birth defects surveillance programs to better estimate the prevalence of clubfoot and investigate its risk factors. **METHODS:** The 10 population-based birth defects surveillance programs that participated in this study ascertained 6139 cases of clubfoot from 2001 through 2005. A random sample of 10 controls per case, matched on year and state of birth, was selected from birth certificates. Data on infant and maternal risk factors were collected from birth certificates. Prevalence was calculated by pooling the state-specific data. Conditional logistic regression was used to investigate the association between risk factors and clubfoot. **RESULTS:** The overall prevalence of clubfoot was 1.29 per 1000 livebirths; 1.38 among non-Hispanic whites, 1.30 among Hispanics, and 1.14 among non-Hispanic blacks or African Americans. Maternal age, parity, education, and marital status were significantly associated with clubfoot. Maternal smoking and diabetes also showed significant associations. Several of these observed associations were consistent between surveillance programs. **CONCLUSIONS:** We estimated the prevalence of clubfoot using data from several birth defects programs, representing one-quarter of all births in the United States. Our findings underline the importance of birth defects surveillance programs and their utility in monitoring population-based prevalence and investigating risk factors. *Birth Defects Research (Part A) 85:897–904, 2009.* © 2009 Wiley-Liss, Inc.

Key words: clubfoot; talipes equinovarus; birth defects surveillance

INTRODUCTION

Clubfoot, or congenital talipes equinovarus, is one of the most common birth defects, with a prevalence of approximately 1 per 1000 livebirths (Wynne-Davies, 1965; Ching et al., 1969; Danielsson, 1992; Byron-Scott et al., 2005). If left untreated, clubfoot can prevent the development of a normal gait, resulting in a lifetime disability. Modern treatments of clubfoot, such as the Ponseti method, use manipulation and immobilization by casting the affected foot and can reduce the need for surgery. Nonetheless, many children still undergo surgical procedures, and disability can occur despite such treatments (Miedzybrodzka, 2003).

Differences in birth prevalence have been reported between racial and ethnic groups, with 6.8 cases per 1000 livebirths among Polynesian populations, 1.12 per 1000 livebirths among white populations, 0.76 per 1000 livebirths among Hispanic populations, and 0.39 per 1000 live births among Chinese populations (Ching et al., 1969; Chung et al., 1969; Moorthi et al., 2005). Regardless of the population, clubfoot consistently demonstrates a male-to-female ratio of 2:1, and bilateral involvement in approximately half of all cases. Among unilateral cases,

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the right foot is affected more frequently (Lochmiller et al., 1998; Wallander et al., 2006). A decreasing trend in the prevalence of clubfoot without a neural tube defect was reported by the Metropolitan Atlanta Congenital Defects Program over a 30-year period (Correa et al., 2007).

The causes of most instances of clubfoot have remained unclear, but for idiopathic clubfoot there is likely etiologic heterogeneity. Several maternal and environmental risk factors have been implicated in the development of clubfoot, although reported findings for many of these have been inconclusive or inadequately studied. Findings regarding maternal age, maternal education, marital status, and parity have been inconsistent, showing differing associations with idiopathic talipes equinovarus (Alderman et al., 1991; Hollier et al., 2000; Carey et al., 2005; Cardy et al., 2007). Other risk factors such as prenatal care and Medicaid use have been studied less frequently (Dickinson et al., 2008).

Studies of regional variations have been limited to relatively similar geographic areas, providing little room for comparison, although a nationwide study in Sweden and a statewide study in Texas observed significant differences in prevalence based on region of residence (Moorthi et al., 2005; Wallander et al., 2006).

Previous studies of clubfoot in the United States have been limited by small sample sizes and confined to individual surveillance programs. The aim of this study is to pool data from several population-based birth defects surveillance programs to better estimate the prevalence of clubfoot and further analyze several of its proposed demographic risk factors. Previously unexamined risk factors, such as diabetes, and variability in prevalence and risk factors between surveillance programs will also be investigated.

METHODS

Data Collection

A population-based case-control study was designed and a call for data, sponsored by the National Birth Defects Prevention Network (NBDPN), was sent to state population-based birth defects surveillance programs inviting them to participate in a collaborative project on clubfoot. The participating surveillance programs were five registries using active case ascertainment methodologies (Metropolitan Atlanta, Iowa, North Carolina, Puerto Rico, and Texas) and five using passive case ascertainment methodologies (Colorado, New York, Rhode Island, Tennessee, and West Virginia); collectively, these programs covered a surveillance population of over 900,000 births per year. Livebirth cases of clubfoot were ascertained for 2001 through 2005 and had diagnoses of either talipes equinovarus (ICD-9/CDC-BPA: 754.51/754.50) or clubfoot not otherwise specified (NOS) (ICD-9/CDC-BPA: 754.70/754.73); four programs also ascertained cases among stillbirths and elective terminations. Cases with anencephalus, spina bifida, encephalocele, chromosomal abnormalities, lower limb deficiencies, or bilateral absence of the kidneys were excluded from the study. Control infants, who were livebirths without major congenital malformations, were selected randomly using birth certificate data to achieve a ratio of 10 control infants per case matched to birth year and surveillance area; additionally, the congenital malformation status of the control infants was verified against the birth defects surveillance program database. Case information, including defect diagnosis, laterality of the defect, prenatal diagnosis, and pregnancy outcome, was requested from the birth defects registries. Data on infant and maternal health and demographics were collected from birth certificates. Infant variables collected from the birth certificates included month and year of birth, sex, gestational age, birthweight, and plurality. Maternal and pregnancy information collected included race or ethnicity, age, month and year of conception, parity, gravidity, presentation at birth, mode of delivery, tobacco use during pregnancy, diabetes, prenatal care, education, marital status, and type of health insurance.

Statistical Analyses

The overall prevalence of clubfoot was estimated by pooling data from all participating programs. Prevalence by program, year, infant sex, maternal race, and maternal age categories were estimated likewise. Ninety-five percent confidence intervals (95% CIs) for the prevalence were estimated using the binomial distribution. The Cochrane-Armitage test was used to describe the trend in prevalence over the five-year period studied. Descriptive analyses of cases and controls were performed using conditional logistic regression (so as to account for the frequency-matched design) to estimate the state-specific crude odds ratios (ORs) and the pooled estimates between variables of interest and clubfoot. Programs unable to provide information for particular variables were excluded from that subset of analyses. Multivariable analyses were performed using conditional logistic regression to estimate adjusted odds ratios (aORs). Data analyses were performed using SAS 9.1 (SAS Institute Inc., Cary, NC).

RESULTS

Ten birth defects surveillance programs, covering over 4.7 million livebirths during the period 2001 through 2005, participated in the study. The programs identified a total of 6139 cases with talipes equinovarus or clubfoot, NOS over the five-year period. Among cases with data on laterality, bilateral clubfoot was present among 54.1% (n = 2149); among unilateral cases, the right foot was affected more frequently (51.5%, n = 940) than the left (47.8%, n = 873); unspecified unilaterality occurred among 0.7% (n = 13) of cases. The laterality of the defect was available from six programs.

The overall prevalence of clubfoot during the five-year period was 1.29 per 1000 livebirths. There was substantial variability in the estimates of clubfoot prevalence between programs, ranging from 1.73 per 1000 livebirths in Colorado to 0.95 per 1000 livebirths in West Virginia (Table 1). The prevalence also varied over the study period, with a prevalence of 1.22 (95% CI: 1.15, 1.29) in 2001 and 1.35 (95% CI: 1.28, 1.43) in 2005 (Table 2). The test for trend was significant, with a p-value equal to 0.02.

With respect to race and ethnicity, prevalence was similar among non-Hispanic whites and Hispanics (1.38 and 1.30 per 1000 livebirths, respectively), somewhat lower among non-Hispanic blacks or African Americans (1.14 per 1000 livebirths), and lowest among Asians (0.87 per

Table 1
Prevalence of Clubfoot per 1000 Livebirths by Surveillance Program, 2001–2005

State	Cases	Livebirths	Prevalence	95% CI
Colorado	591	342,127	1.73	(1.59, 1.87)
Tennessee	673	395,879	1.70	(1.57, 1.83)
Iowa[a,b]	292	190,947	1.53	(1.35, 1.70)
Texas[a,b]	2452	1,881,813	1.30	(1.25, 1.35)
Rhode Island	77	61,396	1.25	(0.97, 1.53)
New York	755	653,291	1.16	(1.07, 1.24)
Puerto Rico[a,b]	294	261,583	1.12	(1.00, 1.25)
North Carolina[a]	646	596,534	1.08	(1.00, 1.17)
Metropolitan Atlanta[a,b]	260	257,255	1.01	(0.89, 1.13)
West Virginia	99	103,886	0.95	(0.77, 1.14)
Total	6139	4,744,711	1.29	(1.26, 1.33)

[a]Active case ascertainment.
[b]Case ascertainment included spontaneous abortions, stillbirths, and elective terminations.
CI, confidence interval.

1000 livebirths). Native Americans had the highest prevalence at 1.46 per 1000 livebirths (95% CI: 0.95, 1.97); however, based on only 31 cases, the confidence interval was wide (Table 2).

Descriptive statistics regarding possible risk factors for clubfoot are presented in Table 3. Male sex was strongly associated with the risk of clubfoot (OR: 1.67, 95% CI: 1.58, 1.76). Other infant factors that showed a strong association with the risk of clubfoot were preterm birth, low birthweight, and breech presentation. Among maternal risk factors, parity was moderately associated with clubfoot, with multiparous mothers having a decreased risk. Young maternal age (younger than 23 years of age) was weakly associated with an increased risk compared to older maternal age (23 through 35 years of age) (OR: 1.14, 95% CI: 1.08, 1.21). Several sociodemographic factors, including marital status, education, and prenatal care, were moderately associated with clubfoot. The risk of clubfoot decreased as maternal education level increased. Mothers with at least a college education had the lowest risk compared to those with less than a high school education (OR: 0.69, 95% CI: 0.64, 0.75). Medicaid use showed a significant association with clubfoot (OR: 1.31, 95% CI: 1.20, 1.42); however, information regarding payer methods was unavailable for many programs.

Demographic factors that demonstrated fairly consistent odds ratios from state to state included male sex, Hispanic ethnicity, young maternal age, and nulliparity. Those displaying greater variability between programs included birthweight, marital status, and prenatal care. Point estimates of odds ratios for maternal college education compared to maternal high school education remained fairly consistent (ranging from 0.75 to 0.90), with the exception of those reported by two programs: one reported a lower odds ratio of 0.43, and one reported a higher odds ratio of 1.14 (Fig. 1).

Maternal smoking information on cigarettes smoked per day was collected from birth certificates. Among control mothers, 9.6% reported smoking during pregnancy. The percentage of control mothers reporting smoking varied from program to program, from 0.4% in Puerto Rico to 22% in West Virginia. Because of the likelihood of underreporting, Puerto Rico was excluded from the smoking analyses, although this exclusion does not preclude the possibility that smoking might have been underreported in other states as well. Compared to nonsmoking mothers, light-to-moderate smoking mothers (those smoking 10 or fewer cigarettes per day) had an increased risk of having an infant with clubfoot (OR: 1.45, 95% CI: 1.32, 1.60). Heavy smokers (more than 10 cigarettes per day) had an even larger increase in risk (OR: 1.88, 95% CI: 1.64, 2.14). State-specific odds ratios for the association between light-to-moderate smoking and clubfoot were above the null for seven of the nine surveillance programs used in the smoking analysis, whereas heavy smoking was associated strongly with an increased risk among all programs, with estimates ranging from 1.37 to 5.33 (Fig. 2).

Maternal diabetes was significantly associated with clubfoot. Clubfoot risk was increased more than twofold for women with pregestational diabetes (OR: 2.39, 95% CI: 1.60, 3.57), whereas the increase in risk associated with gestational diabetes was modest (OR: 1.40, 95% CI: 1.13, 1.72). Odds ratios for pregestational and gestational diabetes showed consistency from program to program, with all estimates for the association between pregestational diabetes and clubfoot above those of gestational diabetes and clubfoot (Fig. 2).

Adjusted odds ratios for several sociodemographic characteristics are presented in Table 4. Variables in the model were maternal race/ethnicity, maternal age, parity, maternal smoking, and maternal education. Other variables that were considered, but not included because of missing data from several programs or years, were marital status, prenatal care, and Medicaid use. Associations with race, parity, maternal education, and maternal smoking previously observed in the unadjusted analyses remained similar in the multivariate analyses. The risk of clubfoot among Hispanics compared to whites decreased slightly, making the finding significant (aOR: 0.92, 95% CI: 0.85, 0.99). Associations with maternal age changed in the adjusted model; young maternal age became associated with a decreased risk of clubfoot (aOR: 0.90, 95% CI: 0.83, 0.96), compared to an increased risk in the univariate analyses.

Table 2
Prevalence of Clubfoot per 1,000 Livebirths by Year and Maternal Race/Ethnicity, 2001–2005

Characteristics	Cases	Livebirths	Prevalence	95% CI
Birth year				
2001	1143	939,211	1.22	(1.15, 1.29)
2002	1211	942,156	1.29	(1.21, 1.36)
2003	1257	951,289	1.32	(1.25, 1.39)
2004	1228	951,057	1.29	(1.22, 1.36)
2005	1300	960,998	1.35	(1.28, 1.43)
Maternal race or ethnicity				
White, non-Hispanic	3329	2,417,338	1.38	(1.33, 1.42)
Black, non-Hispanic	703	618,175	1.14	(1.05, 1.22)
Hispanic	1634	1,261,274	1.30	(1.23, 1.36)
Asian	121	139,003	0.87	(0.72, 1.03)
American Indian	31	21,246	1.46	(0.95, 1.97)
Other/unknown	321	287,675	1.12	(1.00, 1.24)
Total	6139	4,744,711	1.29	(1.26, 1.33)

CI, confidence interval.

Table 3
Descriptive Statistics of Cases and Controls, 2001–2005

Demographic characteristics	Cases (n = 6,139)	Controls (n = 61,390)	Unadjusted OR (95% CI)
Sex			
Male	3875 (63.1%)	31,193 (50.8%)	1.67 (1.58, 1.76)
Female	2254 (36.7%)	30,197 (49.2%)	1.0 (ref)
Missing	10 (0.2%)	0 (0.0%)	
Maternal race or ethnicity[a]			
White	3329 (57.0%)	31,984 (54.7%)	1.0 (ref)
Black/African American	703 (12.0%)	7609 (13.0%)	0.88 (0.81, 0.96)
Hispanic	1634 (28.0%)	16,570 (28.4%)	0.94 (0.88, 1.00)
Asian	121 (2.1%)	1787 (3.1%)	0.65 (0.54, 0.78)
American Indian	31 (0.5%)	250 (0.4%)	1.19 (0.82, 1.73)
Other	6 (0.1%)	108 (0.2%)	0.53 (0.23, 1.21)
Missing	21 (0.4%)	142 (0.2%)	
Gestational age (weeks)			
<34	544 (8.9%)	1692 (2.8%)	3.68 (3.33, 4.07)
34–36	757 (12.3%)	4720 (7.7%)	1.84 (1.69, 2.00)
≥37	4795 (78.1%)	54,661 (89.0%)	1.0 (ref)
Missing	43 (0.7%)	317 (0.5%)	
Birth weight (gm)			
0–2500	1145 (18.7%)	4869 (7.9%)	2.68 (2.50, 2.88)
>2500	4969 (80.9%)	56,494 (92.0%)	1.0 (ref)
Missing	25 (0.4%)	27 (0.04%)	
Maternal age (years)			
<23	1853 (30.2%)	16,921 (27.6%)	1.14 (1.08, 1.21)
23–34	3533 (57.6%)	36,862 (60.1%)	1.0 (ref)
≥35	744 (12.1%)	7589 (12.4%)	1.02 (0.94, 1.11)
Missing	9 (0.2%)	18 (0.03%)	
Parity			
1	2861 (46.6%)	24,380 (39.7%)	1.0 (ref)
2	1663 (27.1%)	19,743 (32.2%)	0.72 (0.67, 0.76)
3	945 (15.4%)	10,326 (16.8%)	0.78 (0.72, 0.84)
4+	577 (9.4%)	6126 (10.0%)	0.80 (0.73, 0.88)
Missing	93 (1.5%)	815 (1.3%)	
Gravidity			
1	2341 (38.1%)	21,016 (34.2%)	1.0 (ref)
2	1545 (25.2%)	17,735 (28.9%)	0.78 (0.73, 0.84)
3	1072 (17.5%)	11,352 (18.5%)	0.85 (0.78, 0.91)
4+	1037 (16.9%)	10,749 (17.5%)	0.86 (0.80, 0.93)
Missing	144 (2.4%)	538 (0.9%)	
Plurality			
Singleton	5797 (94.4%)	58,887 (95.9%)	1.0 (ref)
Twin +	282 (4.6%)	1890 (3.1%)	1.52 (1.34, 1.73)
Missing	60 (1.0%)	613 (1.0%)	
Maternal smoking[b]			
None	4908 (84.9%)	52,027 (90.0%)	1.0 (ref)
1–10 c/day	533 (9.2%)	3943 (6.8%)	1.45 (1.32, 1.60)
>10 c/day	281 (4.9%)	1624 (2.8%)	1.88 (1.64, 2.14)
Any smoking	814 (14.1%)	5567 (9.6%)	1.57 (1.45, 1.70)
Missing	62 (1.1%)	246 (0.4%)	
Maternal education (yr)			
<12	1713 (27.9%)	14,951 (24.4%)	1.0 (ref)
12	1858 (30.3%)	18,168 (29.6%)	0.89 (0.83, 0.95)
13–15	1254 (20.4%)	12,763 (20.8%)	0.85 (0.79, 0.92)
>16	1195 (19.5%)	14,921 (24.3%)	0.69 (0.64, 0.75)
Missing	119 (1.9%)	587 (1.0%)	
Marital status[c]			
Married	3291 (61.1%)	35,088 (65.2%)	1.0 (ref)
Single	2054 (38.2%)	18,721 (34.8%)	1.17 (1.11, 1.24)
Missing	39 (0.7%)	31 (0.1%)	
Mode			
Spontaneous	3543 (57.7%)	40,490 (66.0%)	1.0 (ref)
Forceps/vacuum	317 (5.2%)	2926 (4.8%)	1.24 (1.10, 1.40)
C-section	2223 (36.2%)	17,738 (28.9%)	1.44 (1.36, 1.52)
Missing	56 (0.9%)	236 (0.4%)	

Table 3
Descriptive Statistics of Cases and Controls, 2001–2005 (Continued)

Demographic characteristics	Cases (n = 6,139)	Controls (n = 61,390)	Unadjusted OR (95% CI)
Breech presentation[d]			
Yes	386 (7.4%)	1865 (3.6%)	2.16 (1.93, 2.42)
Not indicated	4838 (92.6%)	50,375 (96.4%)	1.0 (ref)
Prenatal care[e]			
1st trimester	4380 (77.6%)	45,242 (80.1%)	1.0 (ref)
After 1st trimester	897 (15.9%)	9120 (16.2%)	1.01 (0.94, 1.09)
None	96 (1.7%)	660 (1.2%)	1.49 (1.20, 1.85)
Missing	274 (4.9%)	1448 (2.6%)	
Diabetes type[f]			
Pregestational	30 (1.4%)	130 (0.6%)	2.39 (1.60, 3.57)
Gestational	105 (4.8%)	777 (3.5%)	1.40 (1.13, 1.72)
None	2026 (92.2%)	20,944 (95.3%)	1.0 (ref)
Missing	37 (1.7%)	129 (0.6%)	
Medicaid[g]			
Yes	1150 (45.6%)	10,148 (40.2%)	1.31 (1.20, 1.42)
No	1271 (50.4%)	14,357 (56.9%)	1.0 (ref)
Missing	103 (4.1%)	735 (2.9%)	

Excluded programs and years:
[a]Puerto Rico.
[b]Atlanta (2005), Puerto Rico.
[c]New York.
[d]New York (2001–2003), Puerto Rico, Rhode Island, West Virginia.
[e]Texas (2005).
[f]Atlanta, Iowa, North Carolina, Puerto Rico (2001–2004), Rhode Island, Tennessee (2001–2003), Texas (2001–2004), West Virginia.
[g]Atlanta, Colorado, Iowa, Tennessee (2001–2003), Texas (2001-2004), West Virginia.
CI, confidence interval; OR, odds ratio.

DISCUSSION

In this surveillance study of clubfoot in the United States, we pooled data from 10 population-based surveillance programs to achieve a large sample size and obtain information on several potential risk factors. Participating programs provided a diverse demographic and geographic population for this study. The overall prevalence of clubfoot from 2001 through 2005 was 1.29 per 1000 livebirths. This estimate was within the range of several previously reported estimates of 1.1 per 1000 livebirths (Byron-Scott et al., 2005) and 1.4 per 1000 livebirths (Wallander et al., 2006).

Comparison of prevalence estimates across studies is difficult because of the differing exclusion criteria, case ascertainment methods, and study populations. Issues affecting the estimated prevalence in this study are the inclusion of cases of clubfoot, NOS and the racial and ethnically diverse study population. Prevalence estimates varied by program; some of this variability may be due to differing case ascertainment methods. Although our study spanned only a five-year period, there was a subtle trend of increasing prevalence from 2001 through 2005. This trend was not driven by one specific program; instead, six of the surveillance programs reported slight increases in clubfoot over the five-year period. These findings were inconsistent with those of a previous report of a decline in prevalence from 1968 through 2003 (Correa et al., 2007), but were consistent instead with findings of increasing or unchanging prevalence (Krogsgaard et al., 2006). The cause of the observed trend is unclear, but monitoring the prevalence of clubfoot and its risk factors warrants further attention.

The diversity of our study population enabled us to compare prevalence estimates across racial and ethnic groups. We observed a similar prevalence of clubfoot among non-Hispanic whites and Hispanics, which has been reported previously (Moorthi et al., 2005; Dickinson et al., 2008). We also observed a lower prevalence among blacks or African Americans compared to whites (Dickinson et al., 2008). Compared to the total livebirth population of the United States, the surveillance population in this study had a higher percentage of Hispanics (28% compared to 23%), and a lower percentage of white non-Hispanics (51% compared to 57%) (NCHS 2001–2005).

The proportion of cases with bilateral clubfoot was similar to those previously reported, even though this information was available for only 65% of all cases. Our results supported male sex as a strong risk factor for clubfoot (Byron-Scott et al., 2005; Carey et al., 2005; Dickinson et al., 2008). Other strong associations were observed between preterm birth, low birthweight, nulliparity, and breech presentation.

The moderate association of education, marital status, maternal age, prenatal care, and Medicaid use with clubfoot suggested a possible sociodemographic component in the etiology of clubfoot. After adjustment for other sociodemographic variables, these associations observed in the univariate analysis remained similar, with the exception of maternal age. The change in the association between maternal age and clubfoot was largely influenced with the addition of maternal education and parity to the model, indicating that education and parity are stronger risk factors for clubfoot than maternal age. Environmental exposures that might have been mediated by socioeconomic status, such as urban residence, are also possible explanations in the pathogenesis of clubfoot (Krogsgaard et al., 2006).

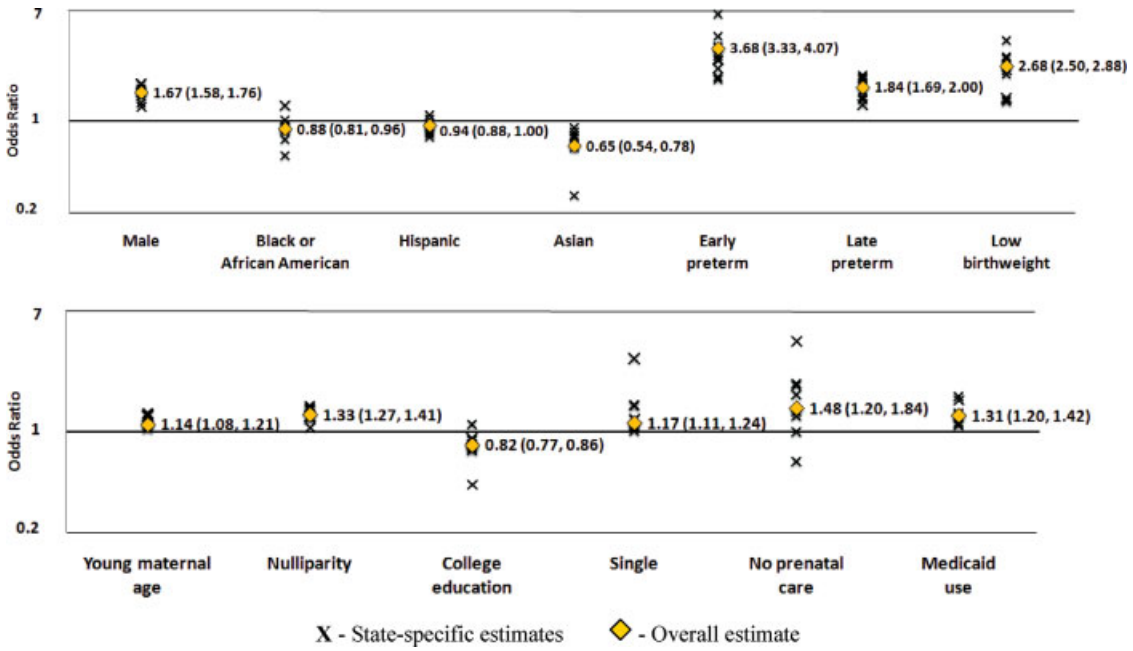

Figure 1. State-specific and weighted odds ratios for clubfoot and specific risk factors, 2001–2005. [Color figure can be viewed in the online issue, which is available at www.interscience.wiley.com.]

Maternal smoking during pregnancy has been one of the more widely studied risk factors for clubfoot. Although a few studies have reported no association, most studies have reported a positive association between maternal smoking and the risk of clubfoot (Van den Eeden et al., 1990; Reefhuis et al., 1998; Honein et al., 2000; Dickinson et al., 2008). The results of this study support the hypothesis that maternal smoking is associated with clubfoot. Compared to that of nonsmokers, the risk of clubfoot was significantly higher among mothers who reported smoking during pregnancy. The crude odds ratio of 1.56 for any smoking during pregnancy was comparable with that previously reported (Reefhuis et al., 1998). Similarly, the presence of a dose-response relationship in this study was consistent with the findings of previous studies of smoking and clubfoot (Honein et al., 2000; Skelly et al., 2002), although not all studies have reported a dose-response relationship (Dickinson et al., 2008). Limitations of the smoking analysis were the use of birth certificates for data collection and lack of information on prepregnancy tobacco use or exposure to environmental tobacco smoke. Even though smoking is likely underreported, smoking data from birth certificates are useful surrogates of actual exposure (Honein et al., 2001). A comparison of maternal smoking reported on birth certificates with that reported through the Pregnancy Risk Assessment Monitoring System (PRAMS) survey showed good correlation and provided little evidence for systematic error (Dickinson et al., 2008).

Both pregestational and gestational diabetes were associated with clubfoot; the risk of clubfoot significantly higher among women with pregestational diabetes compared to those with gestational diabetes. The increased overall risk of birth defects among women with pregestational diabetes compared to women with gestational diabetes has been documented (Correa et al., 2008). The association between diabetes and clubfoot observed in

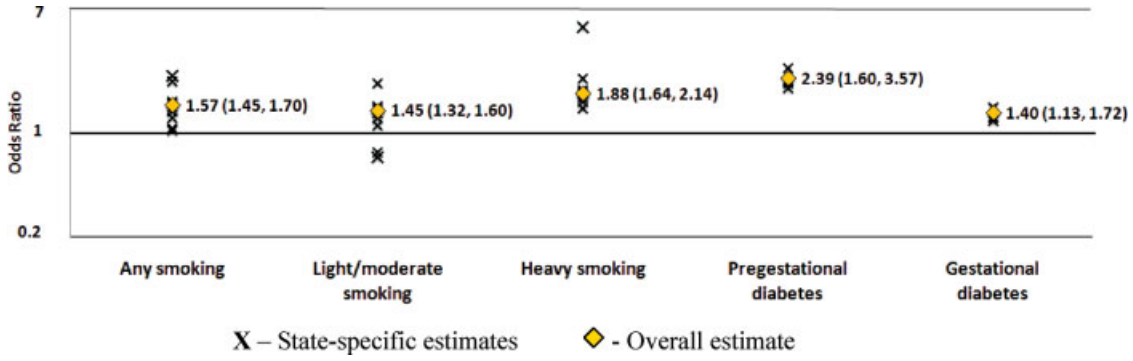

Figure 2. State-specific and weighted odds ratios for clubfoot and specific risk factors, 2001–2005. [Color figure can be viewed in the online issue, which is available at www.interscience.wiley.com.]

Table 4
Multivariable Adjusted Odds Ratios, 2001–2005

Sociodemographic characteristics	Adjusted OR[a] (95% CI)
Maternal race or ethnicity	
White	1.0 (ref)
Black	0.88 (0.80, 0.96)
Hispanic	0.92 (0.85, 0.99)
Asian	0.72 (0.60, 0.87)
Native American	1.10 (0.75, 1.63)
Maternal age (year)	
<23	0.90 (0.83, 0.96)
23–34	1.0 (ref)
35+	1.09 (0.99, 1.19)
Parity	
1	1.0 (ref)
2	0.69 (0.64, 0.74)
3	0.71 (0.65, 0.77)
4+	0.68 (0.61, 0.75)
Maternal smoking	
None	1.0 (ref)
1–10 c/day	1.35 (1.22, 1.49)
>10 c/day	1.76 (1.53, 2.01)
Maternal education (year)	
<12	1.0 (ref)
12	0.92 (0.85, 0.99)
13–15	0.86 (0.79, 0.94)
16+	0.68 (0.62, 0.76)

[a]Adjusted for all other variables in the table. Puerto Rico excluded from multivariate analyses.

this study might have been underestimated, given the likely underreporting of diabetes on vital records (Saydah et al., 2004).

A limitation of our study was that analyses were based on coded data from several surveillance programs. Verbatim descriptions were unavailable from the majority of the participating programs limiting case classification to defect codes. Consequently, we likely based our prevalence estimates on a heterogeneous group of clubfoot cases with varying pathogenic mechanisms. Other foot anomalies coded as clubfoot at birth may have also been included, thereby possibly overestimating the prevalence of clubfoot. Because of our exclusion criteria, the majority of our case group was expected to consist of isolated cases. It is possible that the inclusion of nonisolated cases diluted observed associations with some risk factors given the role of other etiologies in these instances. There was variability in case ascertainment methodology among participating programs, with both active surveillance methods and passive surveillance methods employed. Case identification methods remain quite different between active and passive surveillance systems, which may account for variation in prevalence for certain defects between states (Hobbs et al., 2001). The variation in prevalence estimates among just the active programs in our study was consistent with that of a previous study of 21 birth defects among 11 active surveillance programs (Canfield et al., 2006). Another limitation regarding case ascertainment was the inconsistent inclusion of cases depending on pregnancy outcome. Four of the participating programs included cases who were spontaneous abortions, stillbirths, or elective terminations, while the remaining programs limited cases to livebirths only. Reported cases that resulted in a pregnancy outcome other than a livebirth were rare (<1%) and were retained in the study. Inclusion of these cases did not alter the overall prevalence estimate. This finding was consistent with a previous study reporting that 1.8% of cases with isolated talipes equinovarus resulted in an outcome other than a livebirth (Öfferdal et al., 2007).

Another limitation was the use of birth certificate data for the collection of several variables of interest. The National Center for Health Statistics released an updated version of the birth certificate in 2003. The new version allowed for more detailed data collection on variables such as race and ethnicity, presentation at birth, maternal smoking, diabetes, and payment information. During the study period, some states implemented the new birth certificate, causing a change in the data collection and coding. Artifacts resulting from the use of the new birth certificate varied by surveillance program, but included changes in racial and ethnic distributions and increases in reported diabetes and smoking. The matched study design and analyses should have accounted for these differences in birth certificate data by year and program.

The strengths of this study included the participation of 10 population-based birth defects registries and a large sample size of over 6000 cases from a total livebirth population of 4.7 million. The availability of data from multiple programs allowed for the comparison of several risk factors across a range of surveillance areas, and we present program-specific risk factor to permit comparisons across programs. Risk factors demonstrating little variation across programs might indicate possible biologic causes of clubfoot, while others showing large amounts of variation provide possible evidence of environmental influences on clubfoot or suggest inconsistencies in coding and ascertainment across surveillance systems.

By pooling data from multiple programs, a surveillance population of nearly 1 million livebirths per year, representing almost a quarter of all births in the United States, was achieved. Our findings underline the importance of birth defects surveillance programs and their utility in investigating potential risk factors. Multistate studies provide ample statistical power to investigate several risk factors and offer the opportunity to identify variation between surveillance areas.

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